



PATENT

Our Docket: 066654-604 (P-LJ 4575)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Ruoslahti et al.

) Examiner: M. Yu

) Group Art Unit: 1642

Serial No.: 09/765,086

Filed: January 17, 2001

For: CHIMERIC PROSTATE-HOMING
PEPTIDES WITH PRO-APOPTOTIC
ACTIVITY

ASST COMMISSIONER OF PATENTS
WASHINGTON, D.C. 20231

Sir:

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6-12

DECLARATION UNDER 37 C.F.R. § 1.131

I, the undersigned, hereby declare as follows:

1. I am the Erkki Ruoslahti who is named as a co-inventor of the above-identified application.
2. I understand that the claimed invention stands rejected, in part, as allegedly obvious in view of Ellerby et al., "Anti-cancer activity of targeted pro-apoptotic peptides," Nature Medicine 5: 1032-1038 (1999), which was published in September of 1999.
3. This Declaration attests that the claimed invention was made prior to publication of the above Ellerby et al. publication. Documentary evidence in support thereof is attached hereto as Exhibits 1 and 2.

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4. Prior to September of 1999, I supervised construction of a chimeric peptide containing a prostate-homing peptide linked to an antimicrobial peptide and demonstration of selective cell death in prostate following administration of this chimeric peptide.
5. As evidence that we had conceived and obtained a chimeric prostate-homing pro-apoptotic peptide containing the prostate-homing sequence "SMSIARL" and the antimicrobial sequence "(KLAKLAK)₂," I have attached a photocopy of a CaP CURE Research Award proposal submitted by a Senior Research Associate, Wadih Arap, working in my laboratory. The dates on the CaP CURE Research Award Proposal have been redacted but are prior to September of 1999.
6. Specifically, Exhibit 1 attached hereto is a copy of our CaP CURE Research Award Proposal with a facsimile cover sheet indicating that a copy of our proposal was faxed to us by an individual at the CaP CURE organization.
7. The abstract on the "Face Sheet" of the proposal indicates that a prostate-homing peptide was used to deliver a pro-apoptotic peptide to prostate blood vessels and that, following intravenous administration, the prostate-targeted compound induced massive cell death selectively in the prostate. Figures 2 and 3 (page 2) show that peptide SMSIARL homes specifically to the prostate. Page 3, first full paragraph, indicates that the antimicrobial peptide (KLAKLAK)₂ was chosen as a prototype to be targeted by a prostate-homing peptide to prostate blood vessels.
8. As described at page 3, second full paragraph, and shown in Figure 5, the prostate-targeted compound

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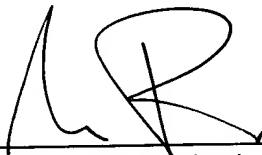
SMSIARLKLAKLAKKLAKLAK was administered to male mice and resulted in specific cell death in the prostate but not in other organs. These results demonstrate that a chimeric peptide containing the prostate-homing peptide SMSIARL and the antimicrobial peptide (KLAKLAK)₂ was prepared and shown to selectively induce cell death in prostate tissue *in vivo*.

9. The results discussed in paragraphs 6 to 8 above show that we had obtained a chimeric prostate-homing pro-apoptotic peptide containing a prostate-homing peptide linked to an antimicrobial peptide prior to September of 1999. The results discussed in paragraphs 6 to 8 above further show that, prior to September of 1999, we had demonstrated selective cell death in prostate tissue *in vivo* following administration of a chimeric peptide containing a prostate-homing peptide linked to an antimicrobial peptide.
10. As additional corroboration of the dates on which the CaP CURE Research Award Proposal was complete, attached as Exhibit 2 is electronic correspondence from Angelica Diega at CaP CURE. Although the dates on the correspondence have been redacted, the correspondence indicates that the research proposal was received by CaP CURE and an award check sent prior to September of 1999.
11. I do not know and do not believe that the invention was in the public prior to the time I conceived of the invention and reduced it to practice and I have never abandoned the application.

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I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

5-19-03
Date



Erkki Ruoslahti



ONE EXECUTED DECLARATION UNDER 37
C.F.R. § 1.131 WITH ATTACHED
EXHIBITS 1 AND 2.

Attorney Client-Matter No.:

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Serial No.: 09/765,086

I hereby certify that this correspondence is being deposited with
the United States Postal Service as first class mail in an
envelope addressed to: Commissioner for Patents, Mail Stop RCE,
P.O. Box 1450, Alexandria, VA 22313-1450, on June 2, 2003.

By Andrea L. Gashler
Andrea L. Gashler, Reg. No. 41,029

June 2, 2003
Date of Signature